SAFETY AND EFFICACY OF IRON SUCROSE COMPARED TO BLOOD TRANSFUSION IN IRON DEFICIENCY ANAEMIA IN PREGNANCY

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CERTIFICATE

This is to certify that this dissertation titled **"SAFETY AND EFFICACY OF IRON SUCROSE COMPARED TO BLOOD TRANSFUSION IN IRON DEFICIENCY ANAEMIA IN PREGNANCY"** is a bonafide work done by **Dr. K.RAMANEESWARI,** Post Graduate Student, Department of OBSTETRICS AND GYNAECOLOGY, Government Kilpauk Medical College, Chennai-10 under my guidance and supervision in partial fulfillment of regulations of Tamil nadu Dr. M. G. R Medical University, for the award of MD Degree Branch II (Obstetrics And Gynaecology) during the academic period of from May 2009 - April 2011.

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INTRODUCTION

Anaemia during pregnancy is defined by World Health Organization as hemoglobin concentration of < 11gm/dl. It is most often caused by iron deficiency. It is one of the most serious global public health problem, affects 52% of pregnant women in developing and 23% in developed countries. (Cochrane data review)[1]

In under developed countries, anaemia is a major contributory factor to maternal morbidity, mortality and higher perinatal mortality rate.

Anaemia in pregnancy is associated with

1. An increased risk of preterm delivery
2. Low birth weight
3. Maternal mortality

During pregnancy, anaemia is most often (about 80%) caused by iron deficiency and occasionally by more complex conditions involving deficient production or accelerated destruction of erythrocytes.

Iron is an essential component of hemoglobin as it is the oxygen carrying pigment in blood. The pregnant women needs 1000mg of iron all through pregnancy i.e. 3.5mg / day to maintain iron balance. The demand during later half of pregnancy and for several weeks after delivery increases to about 6.7mg /day.

Early pregnancy - 2.5 mg / day

20-32 Weeks - 5.5 mg / day

32 weeks onwards - 6-8 mg / day

Iron deficiency is the most frequent nutritional deficiency disorder in the world. Around 600-700 million people world wide have a marked iron deficiency anaemia. In India, despite the measures taken to control anaemia in pregnancy and lactation in the last two decades, the severity of nutritional anaemia contrinues to remain a public health issue of great magnitude (KN Aggarwal et al 2006). [2]

Iron is an important constituent of Hemoglobin, myoglobin and some enzymes. It serves as a carrier of oxygen and electrons and acts as a catalyst for oxygenation and hydroxylation. It also has the ability to catch and release an electron (Fe^{++} / Fe^{+++} cycling).

The marked physiological adjustments occurring in pregnancy, are not sufficient to balance its very marked iron requirements. The reasons for the predominance of this etiological factor are

1. The suboptimal Iron content of diet
2. The insufficient iron stores in the majority of women during their reproductive years.

Iron deficiency anaemia exposes women to an increased risk of blood transfusion during the peripartum period because the parturient can no longer cope with physiologic blood losses of delivery, let alone those associated with hemorrhagic delivery. The risk is equally increased by conditions that incur chronic bleeding during gestation, such as placenta praevia.

There are various treatment modalities for Iron deficiency anaemia during pregnancy. They are

1. Various forms of Iron preparations (Oral tablets, Parenteral Iron)
2. Blood transfusion
3. Erythropoietin

Long term oral treatment can produce side effects, especially digestive ones, which can lead to noncompliance. Parenteral administration by intramuscular injection is a painful alternative with a variable degree of efficacy. Among the iron preparations, iron sucrose iv preparation significantly increases the hematological indices with less side effects and allergic reactions.

Mostly anecdotal evidence suggests that I V and I M iron administration is associated with allergic reactions. compared with I.M iron, IV. iron sucrose significantly increased hematological indices with less side effects. (Cochrane Database syst Rev, 2006;3; CD004736)[3]

Cochrane review conducted (in 2007),randomised controlled trials evaluating the effects of treatments for iron deficiency anaemia in pregnancy, and provide robust valid and useful evidence to inform clinical practice. The study concluded that blood transfusion carries the risk of transmitting parasitic or viral infections including HIV, hepatitis, and chagas disease (trypanosomiasis), despite preventive blood screening. There is also the possibility of bovine spongiform encephalitis, and as yet unknown viral infections. There is also risk of transfusion related acute lung injury (TRALI)[4]

This was the study, conducted in Department of obstetrics and gynaecology Kilpauk Medical College, comparing the safety, efficacy and of 2 different modalities of treatment, iv Iron sucrose and blood transfusion in the treatment of iron deficiency anaemia in pregnancy.

DESCRIPTION OF IRON SUCROSE

Iron sucrose injection, is a brown, sterile, aqueous, complex of polynuclear iron (III)-hydroxide in sucrose for intravenous use. Iron sucrose injection has a molecular weight of approximately 34,000 – 60,000 daltons and a proposed structural formula:

$$[Na_2Fe_5O_8(OH) \cdot 3(H_2O)]_n \cdot m(C_{12}H_{22}O_{11})$$

Where n is the degree of iron polymerization and m is the number of sucrose molecules associated with the iron (III)-hydroxide.

Each ml contains 20 mg elemental iron as iron sucrose in water for injection. Iron sucrose is available in 5 ml single dose vials (100 mg elemental iron per 5 mL) and 10 ml single dose vials (200 mg elemental iron per 10 ml). The drug product contains approximately 30% sucrose w/v (300 mg/mL) and has a pH of 10.5-11.1. The product contains no preservatives. The osmolarity of the injection is 1,250 mOsmol/L.

Therapeutic class: Hematinic

Clinical Pharmacology

Pharmacodynamics& Pharmacokinetics:

Following intravenous administration, iron sucrose is dissociated by the reticuloendothelial system into iron and sucrose. In healthy adults treated with intravenous doses of Iron sucrose, its iron component exhibits first order kinetics with an elimination half-life of 6 hours, total clearance of 1.2 L/h, non-steady state apparent volume of distribution of 10.0 L and steady state apparent volume of distribution of 7.9 L. Since iron disappearance from serum depends on the need for iron in the iron stores and iron utilizing tissues of the body, serum clearance of iron is expected to be more rapid in iron deficient patients treated with Iron sucrose as compared to healthy individuals.

Distribution:

In healthy adults receiving intravenous iron sucrose, its sucrose component appears to distribute mainly in blood and to some extent in extravascular fluid. A study evaluating Iron sucrose containing 100 mg of iron labeled with 52Fe/59Fe in patients with iron deficiency shows that a significant amount of the administered iron distributes in the liver, spleen and bone marrow and that the bone marrow is an iron trapping compartment and not a reversible volume of distribution.

Metabolism and Elimination:

Following intravenous administration of Iron sucrose, iron sucrose is dissociated into iron and sucrose by the reticuloendothelial system. The sucrose component is eliminated mainly by urinary excretion. Some iron also is eliminated in the urine.

Drug-drug Interactions:

Drug-drug interactions involving Iron sucrose have not been studied. However, Iron Sucrose may be expected to reduce the absorption of concomitantly administered oral iron preparations.

AIM OF THE STUDY

1. To compare the efficacy of intravenous iron sucrose with blood transfusion in the treatment of iron deficiency anaemia.

2. To compare the safety of intravenous iron sucrose with blood transfusion in the treatment of iron deficiency anaemia

REVIEW OF LITERATURE

Iron sucrose that releases iron to the endogenous iron – binding proteins with a half life of about 6 hours is not only effective but carry a minimal risk of allergic accident and overload, especially after a comprehensive pretreatment work-up. Postmarketing experience in 25 countries indicates that iron sucrose complex therapy is a valid first- line option for the safe and rapid reversal of iron – deficiency anaemia (Breymann, 2005).[5]

Iron sucrose has been effectively used in pregnancy with highest safety and tolerability among the iron preparations. Good tolerance to iron sucrose is partly due to the low allergenic effect of the sucrose complex, partly due to slow release of elementary iron from the complex. Accumulation of iron sucrose in parenchyma of organs is low compared with iron – dextran or iron – gluconate, while incorporation into the bone marrow for erythropoiesis is considerably faster. By using parenteral iron sucrose in cases of severe iron deficiency, anaemia during pregnancy is treated efficiently and safely according to results and the rate of blood transfusion could be reduced considerably to below 1% of patients per year (perwunyk et al, 2002).[6]

Iron sucrose fits in the criteria for an ideal parenteral iron therapy as defined by Geissser et al in 1992.

A prospective, open controlled study was undertaken to evaluate the safety and efficacy of intravenous iron sucrose complex (ISC) as compared with oral ferrous sulfate in the treatment of iron deficiency anaemia during pregnancy (al Moment et al, 1996).[7] In this study pregnant women with iron deficiency anaemia were sequentially selected from the antenatal clinic and assigned either to ISC (study group) or to ferrous sulfate (control group).

Each study patient was given the total calculated amount of ISC (Hb deficit (g/l) x body weight (kg) x 0.3) in divided dose)200 mg elemental iron in 100 ml normal saline intravenously over 1 hour daily, followed by 10mg /kg to replenish iron stores. Each patient of the control group was given ferrous sulfate 30mg (60 mg elemental iron) orally three times a day. All patients were monitored for adverse effects, clinical and laboratory response. Results: There were 52 patient and 59 control. ISC group achieved a significantly higher Hb level (128.5+/-6.6g/L vs. 111.4 +/- 12.4 g/l in the control group, P< or = 0.001).in a shorter period (6.9 +/- 1.8 weeks vs. 14.9+/- 3.1 weeks in the control group , P<or = 0.001). ISC complex group showed no major side effects while 4 (6%) of the control group, could not tolerate ferrous sulfate, 18(30%) complained of disturbing gastrointestinal symptoms and 18 (30%) had poor compliance. The authors concluded that ISC was safe and effective in the treatment of iron deficiency anaemia during pregnancy.

Similarly iron sucrose therapy in pregnancy was compared with oral iron therapy in a randomized open-label study (AI RA et al, 2005).[8] In this study 90 women with hemoglobin levels between 8 and 10.5g/dL and ferritin values less than 13 mcg /L received either oral iron polymaltose complex (300mg elemental iron per day) or intravenous iron sucrose. The iron sucrose dose was calculated from the following formula: weight before pregnancy (kg) x(110 g/L- actual hemoglobin [g/L] x 0.2+500 mg. Treatment efficacy was assessed by measuring hemoglobin and ferritin on the 14th and 28th days and at delivery, and the hemoglobin on the first postpartum day. Adverse drug reactions, fetal weight, hospitalization time, and blood transfusions were also recorded. Hemoglobin values varied significantly with time between groups (interaction effect, P<.001).

The change in hemoglobin from baseline was significantly higher in the intravenous group than the oral group at each measurement' the changes with respect to subsequent hemoglobin significantly higher in the intravenous group than the oral group at each measurement; the change with respect to subsequent hemoglobin were significantly higher on the 14th (P=.004) and 28th (P=.031) days. Ferritin values were higher in patients receiving intravenous iron throughout pregnancy. No serious adverse drug reaction were observed. Fetal weight and hospitalization time similar in the 2 groups. Blood transfusion was required for only one patient in the oral

group. Thus, intravenous iron treated iron – deficiency anaemia of pregnancy and restored iron stores faster and more effectively than oral iron, with no serious adverse reactions.

Intravenous iron sucrose therapy was compared with intramuscular iron sorbitol in prospective comparative study in 60 pregnant women with IDA with the gestational age of 12-34 weeks (Wali et al, 2002).[9] Patients were divided into three groups A, B and C. Group A(n=15) received intravenous iron sucrose in a dose calculated using formula: weight before pregnancy (kg) x (110 g/L – actual) hemoglobin [g/L]) x 0.24 +500 mg. Group B(n=20) also received intravenous iron sucrose but dose was calculated as weight before pregnancy (kg) x (110 g/L- actual hemoglobin [g/L[ ) x 0.24 + 200 mg. Group C(n=25) received intra muscular iron sorbitol. After 3 weeks of therapy, Hb increased by 2.8 g/dl (group A) and 1.9g/dl in group B. Prior to delivery (ave:6.6 weeks) there was a total rise in Hb of 3.8g/dl (group A) and 2.4 g/dl (group B). In group C, the Hemoglobin was assessed only prior to delivery and a rise of 1.4 g/dl was observed. Target hemoglobin levels i.e 11 g/dl was achieved by 80% in Group A, 70% in Group B and 28% in Group C by the time of delivery. In conclusion, intravenous iron therapy was found to be safe, convenient and more effective than intramuscular iron therapy in treatment of iron deficiency anaemia during pregnancy.

Hoigne et al (1998)[10] compared safety of iron sucrose with iron dextran. They investigated whether there were differences in the frequency of ADRs (adverse drug reactions) to parenteral iron preparations. They evaluated different datasets.

1. In 206 patients, 4 probably allergic reactions to i.m. iron dextran were found, one with acute severe dyspnea, cyanosis and flush, 3 with slight generalized, probably allergic reactions. Data from the USA on i.v. iron dextran did not show marked differences in the frequency of ADRs as compared with their data with i.m. administration.
2. A group of 400 otherwise healthy patients of the obstetric department of Zurich University Hospital were treated with i.v. iron sucrose for anaemia due to iron loss during pregnancy or following childbirth. Seven generalized skin reactions, 4 in the form of flush and 3 of common exanthema, occurred
3. In a retrospective study, not a single life threatening reaction was observed during around 8100patient–years with approximately 160,000 ampoules of iron sucrose (With 100 mg elementary iron) ,only 5-7 situations of rapidly reversible blood pressure fall occurred, 10 with flush, and one each with urticaria and vomiting / diarrhea.

Postpartum blood loss is also associated with iron deficiency anaemia. Severe anaemia, unless corrected may prove to be fatal for the mother. Dede et al (2005)[11] conducted a comparative study in 75 puerperal women with iron deficiency anaemia (Hb 9g/dL). Patients were divided into two groups: IV group given iron sucrose IV and oral group given 60 mg elemental iron three times a day. Evaluation was done after 7 days and after 28 days of starting the therapy. Hb, serum ferritin, serum iron, haematocrit, MCV and total serum iron binding capacity were measured. The authors concluded that compared with oral iron therapy, intravenous iron significantly increased serum ferritim levels within a short period of time with fewer incidences of adverse effects than oral iron in postpartum women with iron deficiency anaemia.

Francoise Bayoumeu et al (2005)[12] in their study to compare oral iron versus iron sucrose concluded that apart from being more effective, Iron sucrose achieves the target levels in a short time. This paves the way for other potential indications, such as anaemia discovered late in the pregnancy or in patients who have low iron reserves and present a risk of hemorrhage during peripartum, such as in multiple pregnancy or over distention of the uterus, in hope of avoiding a transfusion. This possibility should be explored.

Al Moment et al[13] conducted a prospective open – label controlled trial in 111 pregnant women with iron deficiency anaemia (Hb :<9 gm/dl)

and divided into 2 groups. Intravenous group (N.55) and intramuscular group. Intravenous iron sucrose was administered as an infusion of single 100 mg dose in normal saline every 1 to 3 days.

Controls received I.M iron dextran (100mg on alternate days) till the calculated dose was reached. Intravenous iron therapy resulted in higher levels of Hb, with the time to achieve maximum Hb in shorter period compared with controls. No serious adverse effects were noted in iron sucrose group whereas 6% of patients could not tolerate I.M iron dextran, who excluded from the study. 30% of patients in the control group had disturbing GI symptoms and 32% were non complaint.

Wali A, MushtaqA, Nilofer.[9] (Journal Pakistan med. Assoc. 2002 sep 52(9) : 392-5) conducted a prospective comparative study, total number of 60 pregnant women with gestational age of 12-34 wks with iron deficiency were included and divided into 2 groups. Group A (N: 30) received intra venous iron sucrose according to recommended dose containing 500mg of iron sucrose for storage Group B (n=30) received intramuscular iron dextran. Mean Hb in group A was 8.0 +/- 1.1gm/dl and in group B was 8.8 +/- 0.9gm/dl. In group A and B, initial Hb was assessed and 3 weeks after therapy which showed an average rise of 2.8gm/dl in group A and 1.4 gm/dl group B. Target Hb level of 11gm/dl was achieved in 80% of group A, 28% of group B patients. In group A one patients had moderate abdominal pain, 2

had weakness and shivering, 3 had phlebitis but none of the patients discontinued the therapy due to adverse effects.In group B majority, complained of pain at the injection site. In which 5 patients dropped out from study due to intolerance. They concluded that I.V iron therapy is safe, convenient and more effective then I.M Iron therapy, hence I.V iron therapy can replace blood transfusion in antenatal period.

Breyman et al[14] conducted a prospective randomised open study evaluated the efficacy and safety of intravenous iron sucrose with or with out recombinant human erythropoietin in correcting iron deficiency anaemia (Hb <10 gm/dl) in pregnant women ie. Gestational age (> 21 weeks) .20 patients received recombinant human erythropoietin 300 IU/Kg and iron sucrose 200mg I.V and 20 patients received I.V iron sucrose 200 mg alone twice weekly for 4 weeks till a target Hb of 11 gm/dl was achieved. There was immediate reticulocyte response and progressive rise in haematocrit in both groups . Higher rise in reticulocyte count and rise in haematocirt was observed in the group that received combination therapy. None required blood transfusion. No serious adverse effects were reported. They concluded that I.V iron sucrose alone should be considered first in iron deficiency anaemia during pregnancy, recombinant human erythropoietin may be considered in severe anaemia requiring rapid correction, not responding to I.V iron sucrose.

Scoff B. Silvestein and George Reodgers.[15]

The increased availability of parenteral iron preparation should decrease the need to use red cell transfusion in patients with iron deficiency anaemia.

Sal-Momen Ak, el al-Mechari A; al – Nuaime L et al in 1996[16] conducted a study comparing I.V iron sucrose and oral ferrous sulphate, they observed that iron sucrose complex group achieved significantly higher Hb level (128.5+/- 6.6mg/dl Vs 111.4 +/- 12.4g/I) in control group. P<or =0.001. Iron sucrose complex showed no major side effects, but 6% of control group could not tolerate ferrous sulphate . 30% had poor compliance in the control group. They concluded that iron sucrose complex is safe and effective in the treatment of iron deficiency anaemia during pregnancy.

Bayoumeu F, subrian – Buisset E, Baka NE et al (2002)[17] American journal of Obst and Gynaecology also observed the effectiveness, safety and tolerability of I.V iron sucrose compared to oral iron for treatment of iron deficiency anaemia in pregnant women.

Gravier A, Descargues G, Marpeace L et al (1999)[18] conducted a study on how to avoid postpartum blood transfusions in Iron deficiency anaemia patients, by treating with I.V Iron sucrose. They concluded that I.V Iron

sucrose is effective in preventing unnecessary blood transfusion in postpartum patients.

Scott B, Silvestein and Geroge M et al (2004),[15] they have observed that increase in Hb first noted after 1 week of irons sucrose administration and serious anaphylactic hypersensitivity 0.002% in I.V iron sucrose group compared 0.6-0.7% in I.M iron dextran group.

Wested S, Beake B, Smedvig E et al[19] studied the effect of intravenous iron sucrose compared with oral ferrous sulphate, they concluded that women who received. I.V iron sucrose replenished their iron stores more rapidly and had more symptomatic relief compared to oral iron.

Iron sucrose is safe to administer in pregnant diabetics who need IV iron supplementation. (Pharmacotherapy. 2007 Mar; 27(3) : 343-50).[20]

Iron sucrose is safe in patients with cardiac problems when they need IV iron supplement (J Am Coll Nutr 1995;14:71-79).[21]

Intravenous iron, treated iron – deficiency anaemia of pregnancy and restored iron stores faster and more effectively than oral iron, with no serious adverse reactions. (ACOG Vol. 106, No. 6, December 2005) [22]

Intravenous iron sucrose increase the Hb level more rapidly than oral ferrous sulphate in women with postpartum iron deficiency anaemia. It also appears to replenish the iron stores more rapidly. (BJOG 2006; N Bhandal, R Russell).[23]

A prospective, open, controlled study , conducted by EJOG concluded that Iron sucrose complex is safe and effective in the treatment of iron deficiency anaemia during pregnancy. (European Journal of Obstetrics & Gynecology and Reproductive Biology 69 (1996) 121-124).[24]

IRON METABOLISM

Most of the iron within the body is found in hemoglobin within erythrocytes (about 1800mg of iron). Iron is stored in macrophages (and to a lesser extent in hepatocytes), which represents the storage pool of iron (about 1600 mg of iron.). Small amounts of iron are found in myoglobin and in plasma (bound to transferrin).Iron is conserved within the body. The typical adult human body contains about 3000 – 4000 mg of iron. Only about 1 mg of iron is lost from the body per day (through blood loss or sloughed mucosal epithelial cells) and must be replaced through the diet. The majority of iron required by the body is acquired by recycling iron from senescent red cells.

Iron is important in human body because of its occurrence in many hemetopoietins such as hemoglobin, myoglobin & cytochromes. Digested in diet as heme or non heme iron. (Harper's illustrated Biochemisty – 26th Ediciton).

Iron

Most of the iron in the diet is in the ferric (fe^{3+}) form, whereas it is the ferrous (Fe^{2+}) form that is absorbed. Fe^{3+} will be converted into Fe2+ by Fe3+ reductase in the brush border of enterocytes (Willima F. Ganong 21st Edition).

Sources and contents of Iron

Milk : Human Milk 0.5 mg

(Litre) Cow's Milk 0.02 – 0.3 mg

Foods : a) Pulses (9-11 mg)

(80-100 mg) cereals (4-11 mg)

b) Meat, Fish (10-25 mg)

c) Ripe Banana (0.9 mg)

Mango (1.3mg)

Melon (7.5 mg)

Iron absorption

Normally greater proportion of dietary heme iron than non heme iron is absorbed reflecting the greater importance of heme as source of iron. (B Jorn Ramussen et al 1974).

Almost all iron absorption occurs in the duodenum. Iron absorption is facilitated by reducing substances like ascorbic acid, Amino acids.

Sugars especially fructose increase the absorption and may contribute to dietary hemosiderin of Bantus, who consume a diet high in sugar.

Iron absorption is inhibited by alkalies, phosphates, phytates (Maize, Wheat), also by mucosal block i.e., gut has a mechanism to prevent entry of excess iron in the body.

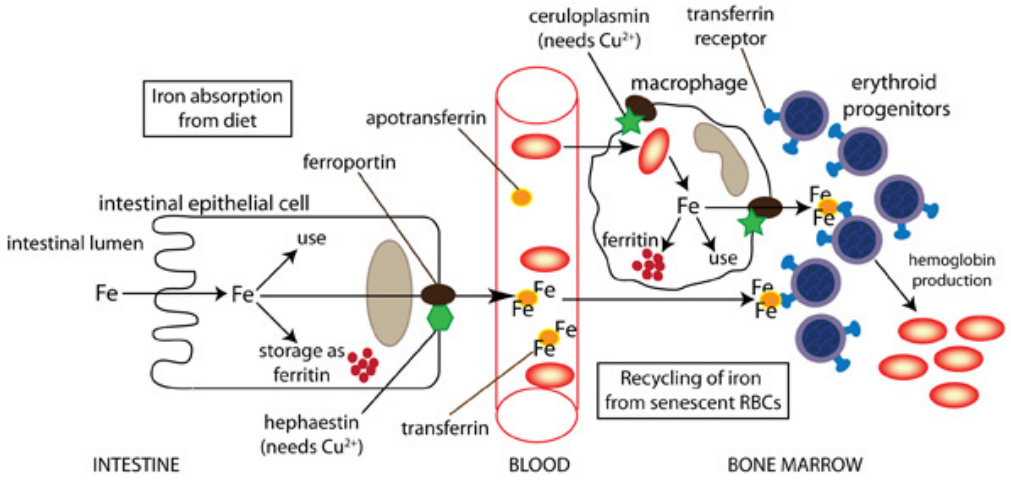
Daily iron requirement for menstruating adult female and pregnancy (last 2 trimesters) is 1-2mg and 3-5 mg respectively.

Good mixed diet provides 10to 15 mg of iron/day. Normal absorption of 10% or so is enough to replace the loss but not able to replace the extra demands of body growth. (Harper's illustrated Biochemistry- 26th Edi)

Iron absorption in gastrointestinal tract

Dietary iron is obtained either from inorganic sources or animal sources (in heme from breakdown of hemoglobin or myoglobin). Dietary iron enters intestinal cells via specific transporters. The iron is then used by the cell (incorporated into enzymes), stored as ferritin (excreted in the feces when the intestinal epithelial cells sloughs) or is transferred to the plasma. Transfer of iron from enterocytes to the transpor4t protein, apotansferrin, occurs through specific iron channels, called ferroportins, and is facilitated by a protein (with ferroxidase activity) called hephaestin. When apotransferrin binds iron, it is called transferrin. Hephaestin contains copper, so copper deficiency will decrease iron absorption (as the iron absorbed from the diet cannot be transferred to plasma). Hepcidin,a main iron regulating

protein, decreases ferroportin and thus decreases iron absorption. Normally transferrin is about 35% saturated with iron.



Heme is transported into the enterocyte by seperate heme transporter (HT), and heme oxidase releases Fe2+ from the heme. Some of the Fe2+ is converted to Fe3+ and bound to ferritin. The rest binds to basolateral Fe2+ transporter ferroportin (FP), and bound to transferrin and stored in the body as ferritin and hemosiderin.

Ferritin containing cells are exfoliated from the mucosal surface at the end of 2-3 days life span. (Conrad and Barton 1981)

Transferrin does not cross that placenta but gives up its iron in chorionic villus, Iron is transferred across the placenta against steep concentration gradient, so it is enzyme dependent. (Waller Stein 1973)

The plasma tranferrin is less than that expected from TIBC. (Vander Heul et al 1972)

Erythorid progenitors obtain iron for hemoglobin synthesis from plasma transferrin or from recycling of senescent erythrocytes by macrophages in bone marrow, spleen and liver. Iron that is in excess of that required for hemoglobin production is stored in macrophages as ferritin, which is oxidized to hemosiderin. These stores can be released from macrophages in times of need (increased erythropoietin).

Iron transfer/recycling

Iron is not free in the circulation but exists as transferrin (bound to apotransferrin). Most of the iron used for red blood cell hemoglobin production is obtained from hemoglobin breakdown of senescent RBCs (called recycling). When red blood cells reach the end of their lifespan (senescent), they are phagocytized by macrophages (in the spleen, liver, bone marrow). Hydrolytic enzymes in macrophages degrade the ingested RBCs and release hemoglobin. Proteolytic digestion of hemoglobin liberates heme and globins. Globins are broken down to amino acids which can be used for

protein production. The iron is released from heme, leaving a porphyrin ring which is converted to bilirubin. Once iron is released from the heme, it is utilized by the cell (iron is an essential component of many enzymes), exported (via ferroportin), or stored as ferritin (like enterocytes). In macrophages, ceruloplasmin (which like hephaestin in intestinal cells also requires copper) is a ferroxidase and facilitate the transfer of macrophage iron to transferrin.

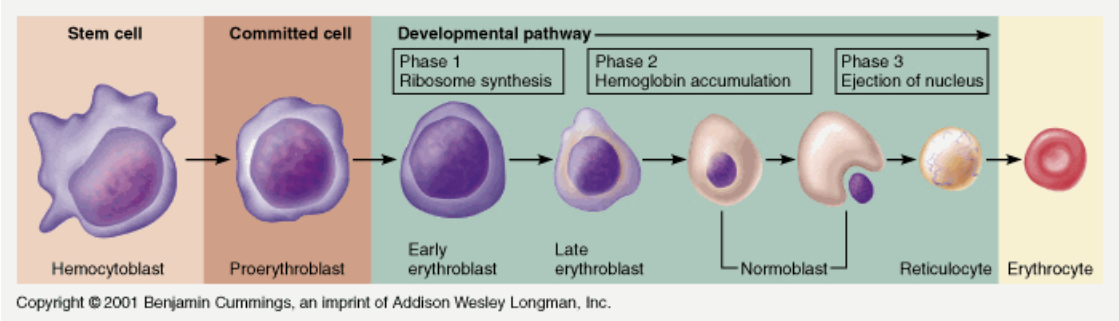
Iron uptake by eythroid progenitors

Transferrin-bound iron (from absorption of dietary iron in the intestine or released by macrophages) binds to transferrin receptors, which are highly expressed on the surface of red cell precursors, and is taken up into the cells where it is used to form hemoglobin. Erythroid progenitors cluster around macrophages in the bone marrow and spleen because they are obtaining their iron (required for hemoglobin synthesis) from these iron-storing cells, as well as from circulating transferrin.

First step is condensation of glycine with succinate, this is iron dependent. Protoporphyrin IX synthesis is inhibited by iron deficiency. (Ganong 21st Edition)

ERYTHROPOIESIS

Erythropoiesis is the development of mature red blood cells (erythrocytes). Like all blood cells, erythroid cells begin as pluripotential stem cells. The first cell that is recognizable as specifically leading down the red cell pathway is the proerythroblast. As development progresses, the nucleus becomes somewhat smaller and the cytoplasm becomes more basophilic, due to the presence of ribosomes. In this stage the cell is called a basophilic erythroblast . The cell will continue to become smaller throughout development. As the cell begins to produce hemoglobin, the cytoplasm attracts both basic and eosin stains, and is called a polychromatophilic erythroblast . The cytoplasm eventually becomes more eosinophilic, and the cell is called a northochromatic erythroblast . This orthochromatic erythroblast will then extrude its nucleus and enter the circulation as a reticulocyte . Reticulocytes are so named because these cells contain reticular networks of polyribosomes. As reticulocytes loose their polyribosomes, they become mature red blood cells.



RBC production is a complex process starting from stem cells all the way to mature RBCs, a process that takes about 25 days.

- RBC is released into circulation from bone marrow, but before release of RBC, it requires incorporation of iron into it.
- Proerythroblast (day 20 of RBC formation) is the stage where incorporation of iron takes place.
- Iron incorporation happens within 24 to 72 hrs window period just before the young RBC is ejected into the circulation.
- Proerythroblasts turns into a mature RBC within 5 days.
- In severe anaemia, the hypoxic state induces high amount of erythropoietin (EPO) secretion. In this high EPO state, the erythropoiesis up to day 20 is accelerated. IV iron in such high EPO state can stimulate erythropoiesis by 5 times normal rates.
- Administration of iron through intravenous route makes available high quantity of elemental iron for incorporation at the proerythroblast stage and hence iron sucrose administration can provide quick Hb rise within 5 to 7 days.

IRON DEFICIENCY ANAEMIA

Iron deficiency anaemia is the most common nutritional deficiency in pregnancy followed by folate deficiency anaemia. Out of 150 million deliveries occurring annually in the world, approximately 6,00,000 women die from the complications of pregnancy. Anaemia is responsible for 40%-60% of maternal deaths in non-industrialized countries. Anaemic mother is more likely to succumb to the ill effects of hemorrhage, be susceptible to infection and suffer from congestive cardiac failure. (Progress in obstet and gynaecology, STUDD volume 15).[25]

WHO criteria for diagnosis of anaemia in pregnancy is Hb content of <11 gm/dl (7.45 mmol/l) and haematocrit of less than33%. CDC (Centers for Disease control, USA)[26] proposes a cut off point of 10.5 gm/dl during the second trimester. (Progress in obstet and gynaecology, STUDD volume 15).

ICMR categories of anaemia.[27]

Category	**Severity**	**Hb level (gm/dl)**
1.	Mild	10.0 – 10.9
2.	Moderate	7.0 – 10.0
3.	Severe	<7.0
4.	Very severe	<4.0

Iron Deficiency Anaemia;

Prevalence of anaemia in pregnancy

Anaemia affects about 18% of women during pregnancy in industrialised countries while in non-industrialised countries, prevalence varies between 35-75% ,average being 56%. Incidence of anaemia in India ranges between 20 and 30% in the middle income group and much higher in low income group (60%) and 70% in rural women.

(Progress in OBG, STUDD volume 15)

Iron Requirements in Pregnancy

Basal iron	-	280mg,
Expansion of red cell mass	-	570mg
Transfer to the fetus	-	200-350mg
Placenta	-	50-150mg
Blood loss at delivery	-	100-250mg

After deducting iron conserved by amenorrhoea (240-480 mg), an additional 500-600 mg of iron is required in pregnancy or 4-6 mg/day of absorbed iron i.e. 2.5 mg/day in early pregnancy, 5.5 mg/day from weeks 20-32 and 6-8 mg/day from weeks 32 onwards.

As absorption is less than 10%, atleast 40-60 mg of iron should be available in the diet.

Causes of high prevalence of Iron deficiency anaemia;

1. Increased iron requirement
2. Dietary habits

Consumption of low bio availability diet, also higher in both Hindu vegetarian and Muslim (Halal Meat eaters), this could be due to loss of significant amounts of heme blood from the Halal meat where the animal is slaughtered by cutting its carotid artery and bled to death.

(Sharma and Soni 1999).

1. Defective iron absorption due to intestinal infection like hook worm, schistosomiasis, chronic malaria.
2. Menorrhagia / Bleeding from the gut due to haemorrhoids.

States of Iron deficiency anaemia;

Stage I : Negative iron balance

Demands for iron exceed the body's ability to absorb iron from diet.

Normal Hb / haematocrit level

Normal RBC indices

Serum Ferritin <20ng/ml

Stage II: Iron deficient Erythropoiesis

When stores become depleted, serum iron begins to fall, total iron binding capacity rises gradually and once the transferrin falls to 15 to 20%, Hb synthesis becomes impaired.

State III : Iron deficiency anaemia

Peripheral picture reveals microcytic and hypochromic cells appearing as vacuolated red blood cells with reticulocytes in circulation. Gradually Hb and haematocrit begins to fall. Transferrin saturation <15%.

Clinical Features

Patient may be asymptomatic especially in mild and moderate anaemia. Patient may complain of weakness, exhaustion, indigestion, loss of appetite, palpitation, dyspnoea, giddiness and edema. Congestive cardiac failure can occur in severe cases.

Signs:

There may be no signs especially in mild anaemia. There may be pallor, glossitis and stomatitis. Patient may have edema due to hypoproteinemia. Soft systolic murmur can be heard in mitral area due to hyperdynamic circulation. There can be fine crepitations at bases of lungs due to congestion.

Effects of anaemia on pregnancy

Maternal effects

Mild anaemia may not have any effect on pregnancy and labour except that the mother who has low iron stores, may become moderate to severely anemic in subsequent pregnancies. Moderate anaemia may cause increased incidence of preterm labour (28.2%), pre-eclampsia (31.2%) and sepsis.

During labour there is an increased incidence of postpartum hemorrhage and congestive cardiac failure.

During puerperium, there is an increased chances of puerperal sepsis, sub involution, failing lactation and venous thrombosis.

Fetal effects

Irrespective of the maternal iron stores, fetus tends to obtain iron from maternal transferrin. But gradually the fetal iron stores becomes depleted. So babies born to anaemic mother should be started on oral iron in the infancy itself.

Iron deficiency anaemia is a significant risk factor for prematurity and low birthweight infants, if it is present in first trimester. In 2^{nd} and 3^{rd} trimester, it had little effect on these fetal outcomes. (School et al).

Lozoff et al observed a significant effect of anaemia on the affective behavior of an anaemic child.

Diagnosis

Although the assessment of iron status in human population is advanced compared with other nutrients, there is still a large uncertainty about absolute diagnosis during pregnancy. (Am J Clin Nutr. 1994: 59 (Suppl) 5025 – 10s).[28]

Parameters	Normal	Negative iron balance	Iron deficient erythropoiesis	Iron deficiency anaemia
Marrow iron stores	1 – 3 +	0 – 1 +	0	0
Serum ferritin (ng/ml)	50-200	<20	<15	<15
TIBC (mg/dl)	300-360	>360	>380	>400
Serum iron (mg/dl)	50-150	Normal	<50	<30
Saturation (%)	30-50	Normal	<20	<10
Marrow sideroblasts (%)	40-60	Normal	<10	<10
RBC protoporphyrin (mg/dl)	30-50	Normal	>100	>200
RBC morphology	Normal	Normal	Normal	Microcytic hypochromic

Red cell indices

Among the Red cell indices, MCV is the first to get reduced and is the most sensitive indicator of iron deficiency anaemia. MCHC is reduced in more severe cases of iron depletion.

	Normal	Iron deficiency anaemia
MCV (fl)	75.96	reduced
MCHC (g/dl)	32.35	reduced

Prophylactic Supplementation

WHO recommendation based on the prevalence of anaemia

< 40% : 60mg elemental iron and 0.4mg of folic acid.

> 40% : supplemented for another 3 months postpartum.

National nutritional anaemia control programme guidelines.

100mg of elemental iron and 0.5mg of folic acid for minimum of 100 days, starting in the 2nd trimester and continued 3 months postpartum.

Treatment of iron deficiency anaemia

Iron deficiency anaemia is the main cause of anaemia during pregnancy. Iron should be the mainstay of therapy oral, parentral or through transfusion.

Breymann 2005 explained that the efficacy of oral or intramuscular iron is limited in many patients, due to dose dependent side effects, lack of compliance and insufficient duodenal iron absorption, and correction of hematological and iron status parameters are still lacking.

Breymann 2005 also stated that transfusion has many problems including transmission of viruses and bacteria, RBC quality can be compromised during storage and the possibility of transmitting prions is an increasing worry.

Breymann 2005 maintained that following I.V iron sucrose administration, it is not necessary to survey the patient (or) monitor their blood pressure, the patient can leave with 100% compliance.

The increased availability of multiple parenteral iron preparations should decrease the need to use red cell transfusions in patients with Iron deficiency anaemia. (Am. J. Hemetol 76 : 76 -78, 2004)[29]

MATERIALS AND METHODS

Study Setting : Kilpauk Medical College Hospital

Department of Obstetrics and Gynaecology

Study Design : Prospective Randomized Control Study

Study Period : November 2009 to October 2010

Sample Size : Determined by Statistical analysis. Statistical analysis done was done by using chi square test & student 't' test & 'p' value in appropriate places.About 100patients were randomized for either Iron sucrose or blood transfusion. A 'p' value less than 0.05 is taken to denote significant relationship.

Inclusion criteria for the patients

Following criterias were utilized in selecting patients for this study

- ❖ Age 18-45 yrs
- ❖ Singleton pregnancy between 28 to 34 wks
- ❖ Hb – 7- 8 gm/dl

Exclusion Criteria

1. Underlying disease such as hypertension, gestational diabetes, heart disease, peptic ulcer.
2. H/o allergy to iron containing medication.
3. H/o other allergic conditions or asthma.

4. Thalassemia.
5. H/o Bleeding tendency.

After confirming iron deficiency anaemia using

- ❖ Hemoglobin
- ❖ Haematocrit
- ❖ MCV
- ❖ Peripheral smear

Antenatal patients with iron deficiency anaemia who fulfilled the above said criteria were randomly allocated into 2 groups. Group I and Group II. each Group contains 50 antenatal patients.

After obtaining an informed consent, a detailed history taking, a complete general examination and detailed obstetric examination were done.

Method of the Study

Calculation of iron requirement

Iron requirement is calculated using the following formula

2.4 x (target Hb – patient Hb) x Pre pregnancy weight (kg) +500 (Storage iron) = mg of elemental iron

Group I patients were given intravenous iron sucrose complex, 100 mg of elemental iron diluted in 100 ml of 0.9% normal saline was infused over 15min, on alternate days until the required dose was infused. Test dose was not given.

Group II patients were given one unit of packed cell transfusion, Hb was reassessed after 48 hours, further transfusions were given until the required Hb was achieved.

Observation

During therapy the following parameters were monitored

1. Vitals (Pulse, BP, Temperature)
2. Adverse effects like nausea / vomiting / abdominal pain, chills etc.
3. Anaphylactic reactions.
4. Urine output

Patients were advised to attend our OPD 2 weeks after therapy and the following parameters were assessed.

1. Symptomatic improvement
2. Hb
3. Haematocrit
4. MCV

Follow up

GA at delivery: preterm / term delivery

RESULTS OF THE STUDY

Table 1

AGE DISTRIBUTION

Age in Years	Group I		Group II		Total %
	No. of Cases	Percentage	No. of Cases	Percentage	
<20	10	20	8	16	18%
21-25	28	56	21	42	49%
26-30	9	18	14	28	23%
>30 yrs	3	6	7	14	10 %
Total	50	100%	50	100	100%

P = 0.271 Not significant

INFERENCE

There is no significant change in the age distribution between the two age Group. Among 100 women studied, 18%,were less than 20 years, 49% of patients belongs to the age Group 21-25 yrs, 23% belong to age Group 26-30 yrs, and 10% belong to age >30 yrs.

The mean age was 23.48 & 25.08 in Group A and Group B respectively.

FIGURE 1

AGE DISTRIBUTION

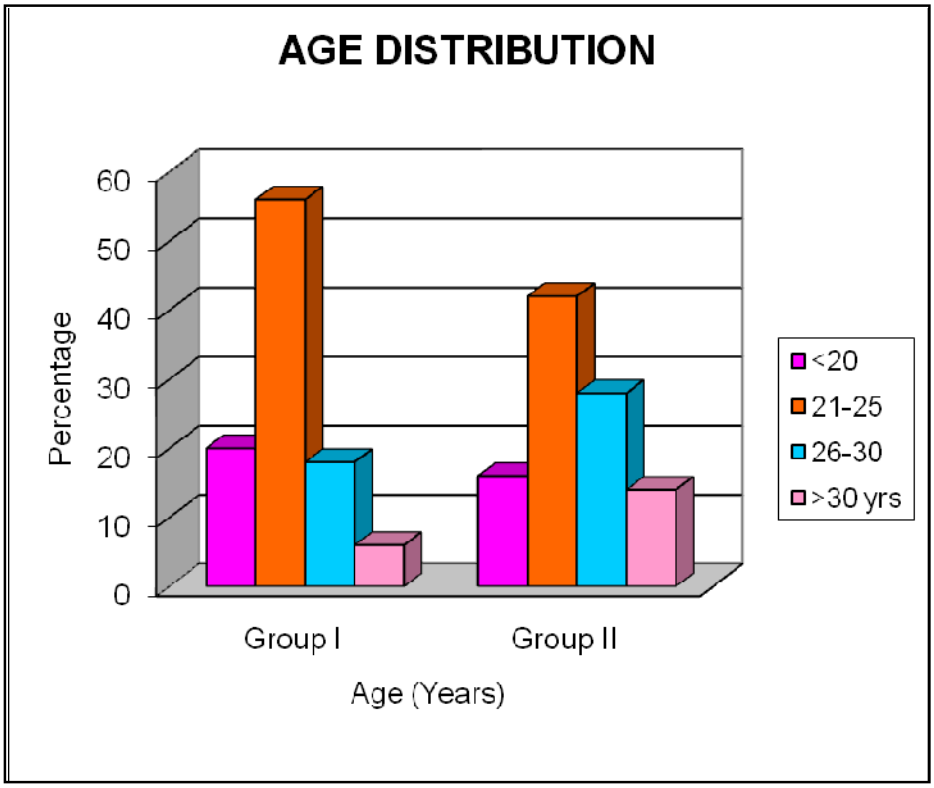


Table 2

BOOKING STATUS

Booking status	Group I		Group II		Total %
	No. of Cases	Percentage	No. of Cases	Percentage	
Booked	18	36	26	52	44%
Unbooked	32	64	24	48	56%
Total	100	100	100	100	100

P = 0.107 Not Significant

INFERENCE

The booking status of both group I and group II were same .

Among the 50 patients in Group I ,36% were booked, 64% were unbooked. In Group II, 52% were booked and 48% were unbooked. There was no significant change in both group.

FIGURE 2

BOOKING STATUS

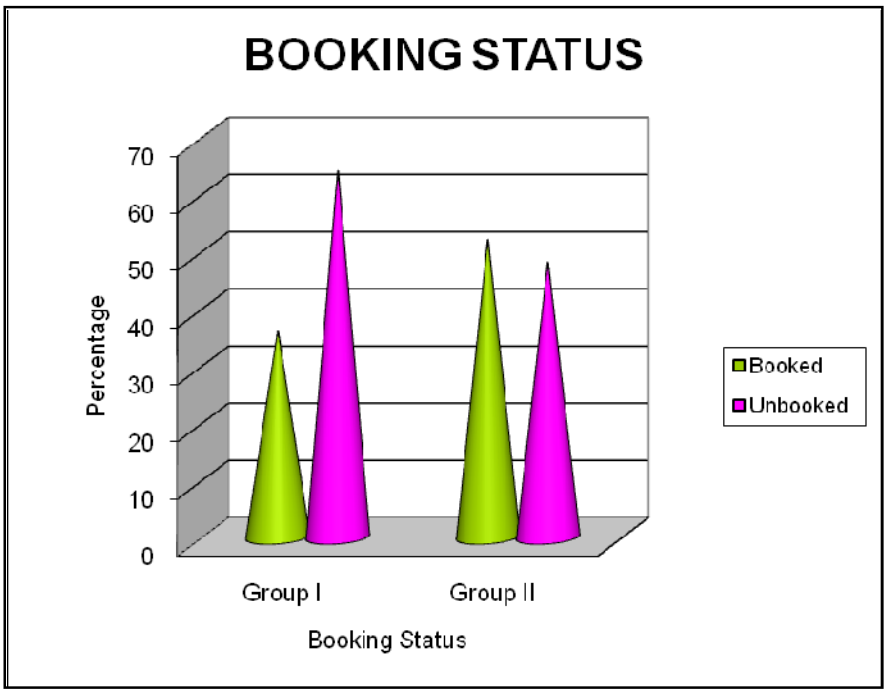


Table 3

OBSTETRIC CODE

GRAVIDA	Group I		Group II		Total %
	No. of Cases	Percentage	No. of Cases	Percentage	
1	24	48	24	48	48%
2	20	40	15	30	35%
3	4	8	6	12	10%
4	2	4	5	10	7%
Total	100	100	100	100	100

P = 0.494 Not Significant

INFERENCE

48% of patients in Group I and 48% of patients in Group II, were primigravida, while only 4% in Group I and 7% Group II were gravid 4. Both primi and multipara were equally distributed in both the Groups.

FIGURE 3

OBSTETRIC SCORE

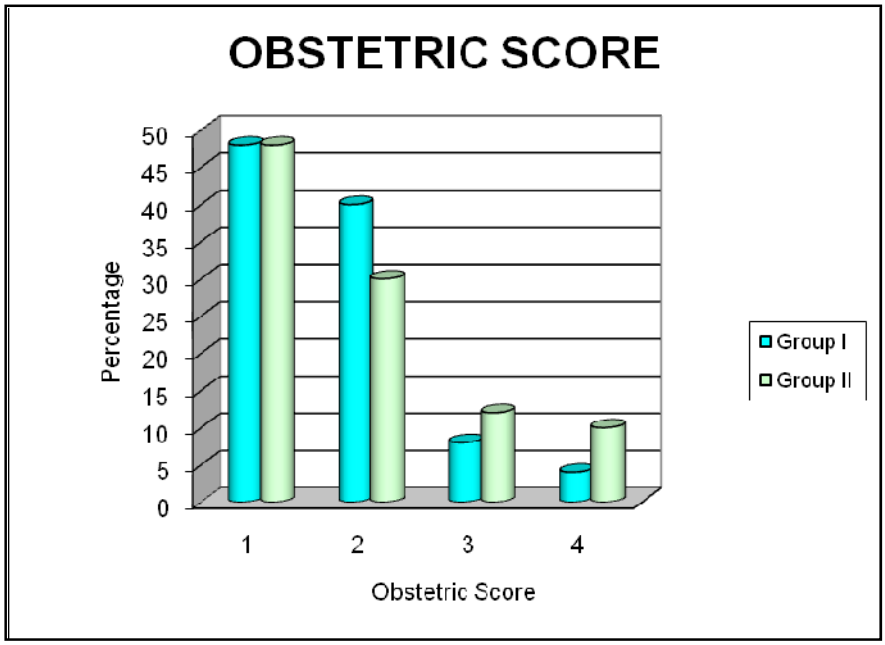


Table 4

SOCIO ECONOMIC STATUS

SOCIO ECONOMIC STATUS	Group I		Group II		Total %
	No. of Cases	Percentage	No. of Cases	Percentage	
Class I	0	0	0	0	0
Class II	0	0	0	0	0
Class III	2	4	5	10	7
Class IV	23	46	23	46	46
Class V	25	50	22	44	47
Total	50	100	50	100	100

P = 0.452 Not Significant

INFERENCE

47% of women belonged to class V socio economic status, 46% belonged to class IV socioeconomic class.

FIGURE 4

SOCIO ECONOMIC STATUS

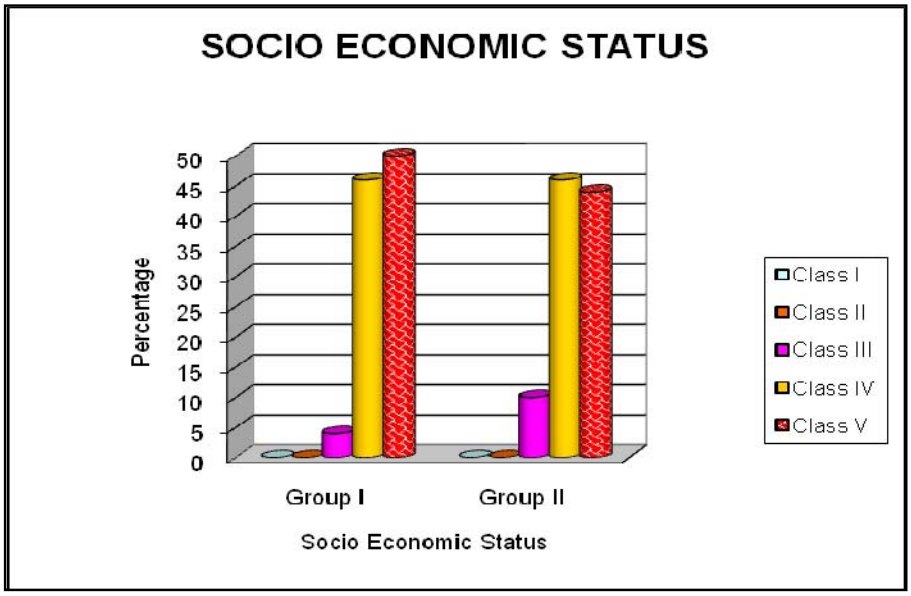


Table 5

Change in Hemoglobin

Hemoglobin (gm/dl)	Group I				Group II				P Value
	N	Mean	S.D	S.E.M	N	Mean	S.D	S.E.M	
Pre Treatment	50	7.498	0.332	0.0469	50	7.55	.374	.0530	0.431
Post Treatment	50	10.943	0.337	0.04767	50	11.09	.501	.07093	0.089
Change in Hb	50	3.44	.420	.0595	50	3.51	.429	.0607	0.417

Not Significant

INFERENCE

Mean Hb in Group I and Group II was 7.498 gm/dl and 7.55 respectively. Post therapy Hb after 2 weeks showed a mean Hb value of 10.943 gm/dl and 11.09gm/dl respectively (P-0.089) which was statistically not significant.

The average rise of Hb was 3.44 gm/dl and 3.51 gm/dl respectively in Group I and Group II (P-0.417) which was statistically not significant.

FIGURE 5

CHANGE IN HEMOGLOBIN

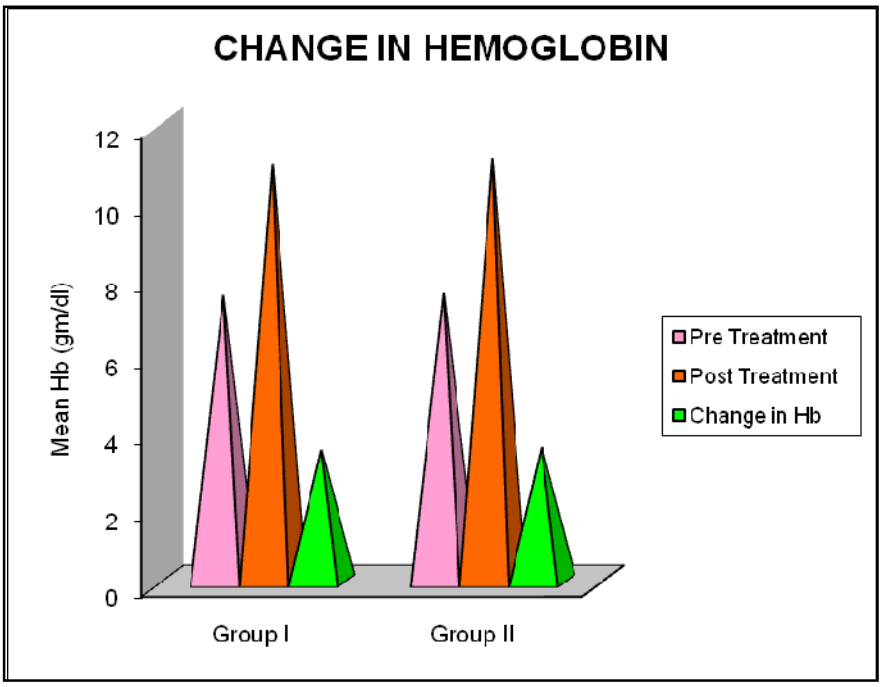


Table 6

CHANGE IN HAEMATOCRIT

Haematocrit (Percentage)	Group I				Group II				P Value
	N	Mean	S.D	S.E.M	N	Mean	S.D	S.E.M	
Pre Treatment	50	28.4	1.39	.196	50	30	1.5	.213	.212
Post Treatment	50	33.99	1.56	.221	50	38	1.25	.1767	.496
Change in Haematocrit	50	5.51	1.77	.250	50	8	1.23	.17509	.072

Not Significant

INFERENCE

Among 100 patients studied, Haematocrit in Group I and Group II was 28.4% and 30.0% respectively. Post therapy Haematocrit after 2 weeks showed a mean Haematocrit value of 33.99% and 38.0% respectively P value is (.496) which was statistically not significant. The average gain of Haematocrit was 5.5% and 8.0% in Group I and Group II respectively, which was statistically not significant.

FIGURE 6

CHANGE IN HAEMATOCRIT

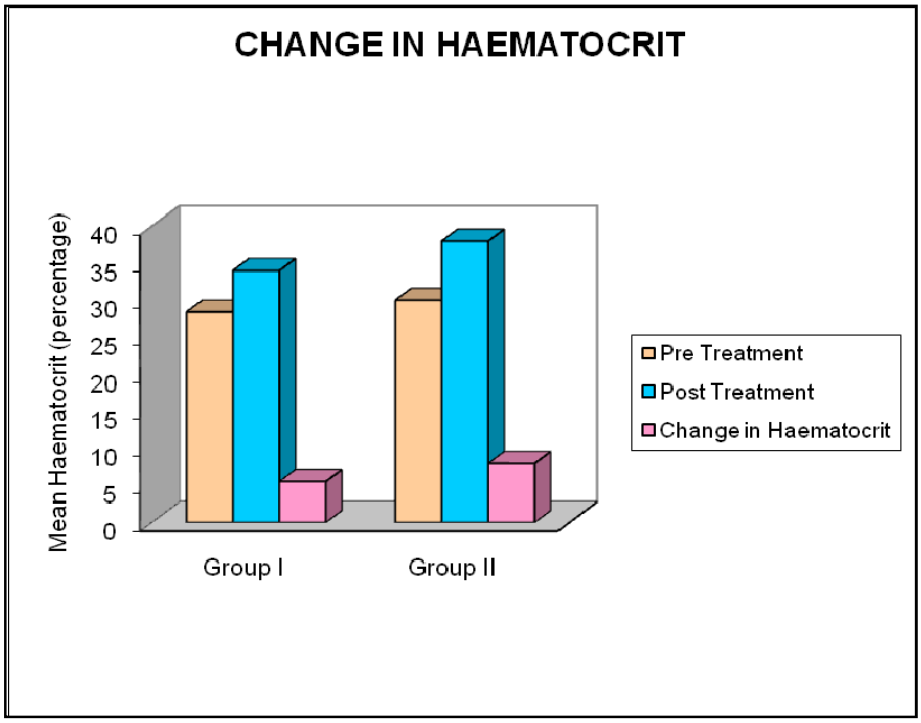


Table 7

CHANGE IN MCV

MCV(fl)	Group I				Group II				P Value
	N	Mean	S.D	S.E.M	N	Mean	S.D	S.E.M	
Pre Treatment	50	69.19	3.707	.524	50	69.03	2.58	.365	0.803
Post Treatment	50	86.69	1.868	.264	50	86.01	1.90	.268	.074
Change in MCV	50	17.496	3.616	.511	50	17.09	2.96	.418	0.547

P= .574 Not Significant

INFERENCE

Among 100 patients studied, Mean MCV in Group I and Group II was 69.19fl and 69.03fl respectively. Post therapy assessment after 2 weeks in Group I and Group II Showed a Mean MCV value of 86.69fl and 86.01fl respectively (P=.574) which was not statistically significant. The average gain in MCV was 17.49 fl and 17.09 fl in Group I and Group II respectively.

FIGURE 7

CHANGE IN MCV

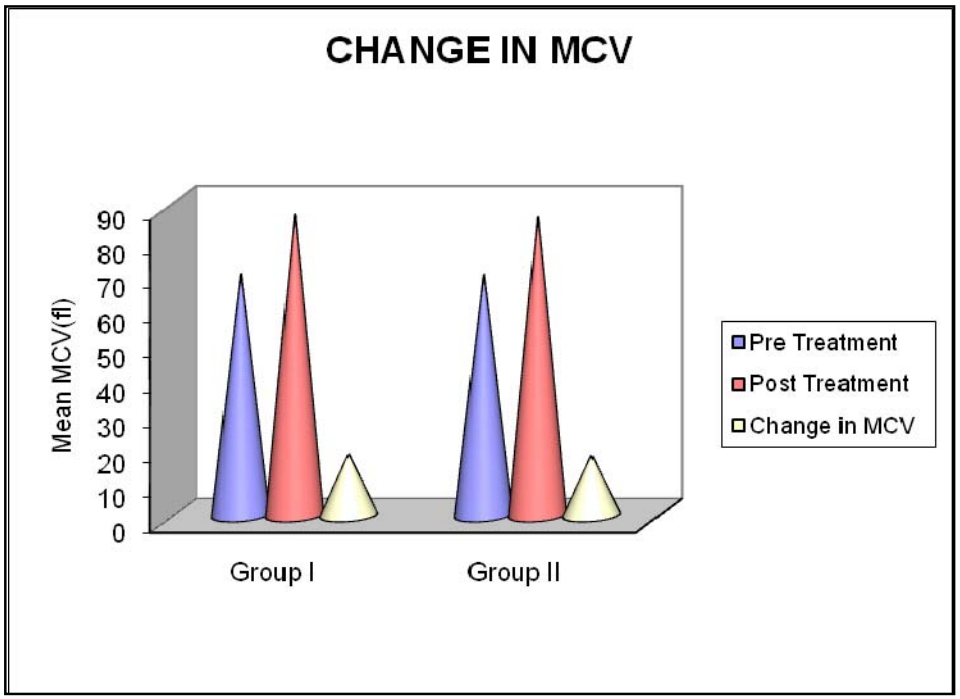


Table 8

SYMPTOMS

Symptoms	Group I	Group II
	No. of .Cases	No. of .Cases
Easy fatiguability and pallor	27	22
Breathlessness and pallor	5	4
Pallor of Skin and Mucus Memb	13	19
Easy fatiguability pallor & breathlessness	5	5
Total	50	50

SYMPTOMATIC IMPROVEMENT

Symptomatic Improvement	Group I (n=50)		Group II (n=50)	
	No. of Cases	Percentage	No. of Cases	Percentage
Easy fatiguability and pallor	27/27	100	22	100
Breathlessness and pallor	5/5	100	4	100
Pallor of Skin and Mucus Memb	13/13	100	19	100
Easy fatiguability pallor & breathlessness	5/5	100	5	100

P value=0. 0627 Not Significant

INFERENCE

In Group I , among 27 patients with easy fatiguability and pallor and 5patients with breathlessness (Grade I) and pallor and 13 patients with only pallor and 5 patients with all the three findings, all (100%) experienced improvement of symptoms after intravenous Iron sucrose therapy.

And in Group II also, among 22 patients with easy fatiguability and pallor , 4 patients with Breathlessness and pallor, 19 patients with only pallor, 5 patients with all the three findings, all (100%) experienced improvement of symptoms after blood transfusion. Thus, there was no statistical significance.

Table 9

ADVERSE EFFECTS

	No. of Cases	**Patients with Adverse effects**	**Patients without Adverse effects**
Group I	50	0	50
Group II	50	22	28

Chi - squre = 28.205 P = 0.000 SIGNIFICANT

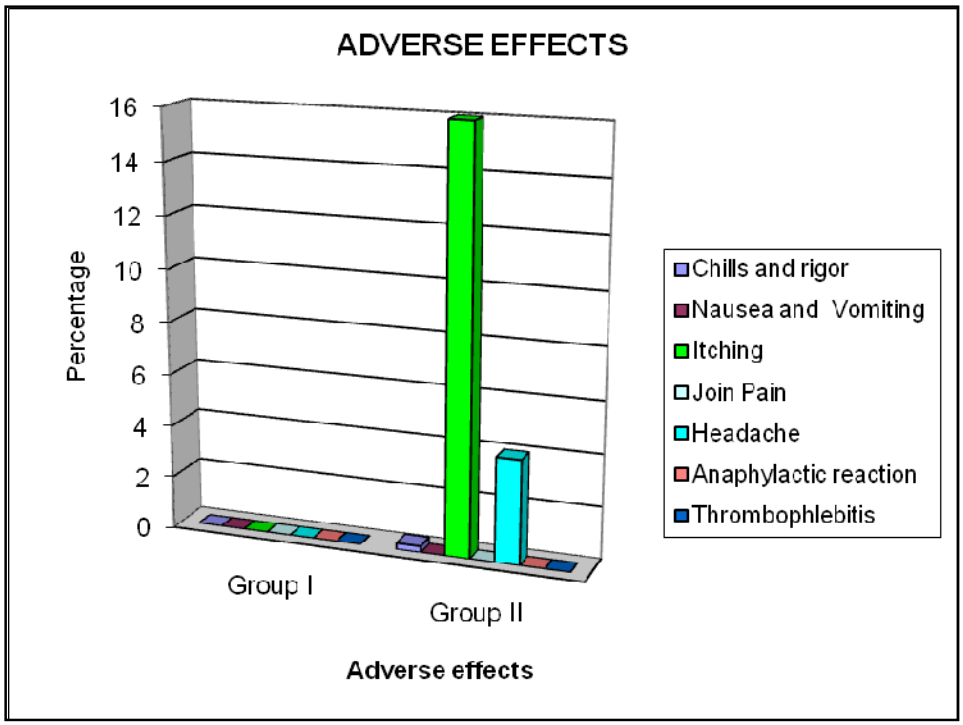
Table 9

ADVERSE EFFECTS

ADVERSE EFFECTS	**Group I**		**Group II**		**Total %**
	No. of Cases	**Percentage**	**No. of Cases**	**Percentage**	
Chills and rigor	0	0	12	24%	12%
Nausea and Vomiting	0	0	0	0	0
Itching	0	0	8	16	8
Join Pain	0	0	0	0	0
Headache	0	0	2	4	2
Anaphylactic reaction	0	0	0	0	0
Thrombophlebitis	0	0	0	0	0

FIGURE 9

ADVERSE EFFECTS



INFERENCE

Among 50 patients studied in Group I, adverse effects were almost nil. But in Group II more adverse effects like headache 2/50 (4%) chills and rigor 12/50 (24%), itching 8/50 (16%) were found. But there was no anaphylactic reactions noted in both the groups P value is 0.000.

Adverse reactions were statistically significant between the two groups studied.

Table 10

GESTATIONAL AGE AT DELIVERY

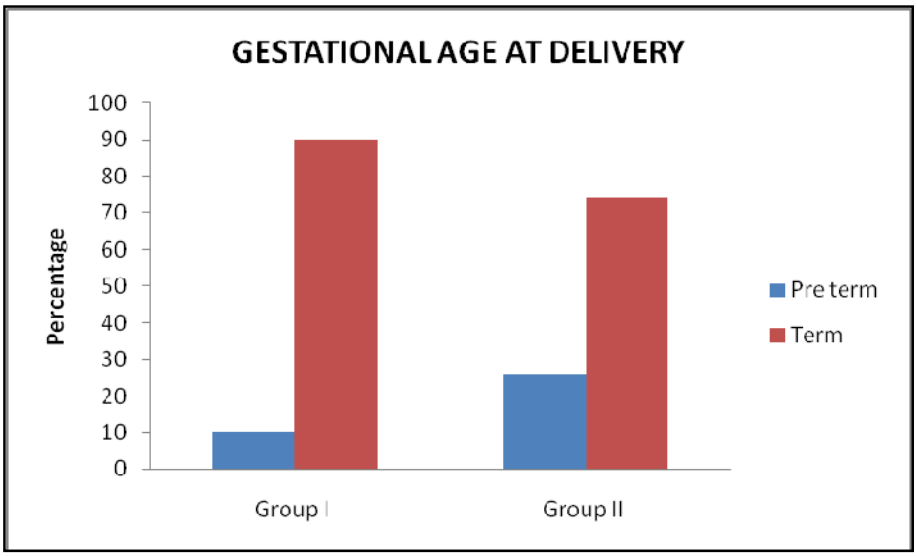
GA at delivery	Group I		Group II	
	No. of .Cases	Percentage	No. of .Cases	Percentage
Pre term	5	10	13	26
Term	45	90	37	74
Total	50	100	50	100

P= 0.01866 Significant

Among 100 patients studied, 10% (5 patients) in Iron sucrose group (Group I), 26% (13 Patients) in blood transfusion group (Group II) delivered preterm. P Value is 0.01866 which was statistically Significant.

FIGURE 10

GESTATIONAL AGE AT DELIVERY



DISCUSSION

In our study 100 antenatal patients with iron deficiency anaemia were selected according to the inclusion and exclusion criteria stated in methodology. They were divided into 2 groups (50 patients each)

In Group I, 50 Antenatal patients were given injection Iron sucrose 100 mg IV Infusion over 15-20 minutes on alternate days, until the calculated does was infused

In Group II, 50 Antenatal patients were given blood transfusion (Packed cell) once in 2 days until the required hemoglobin was achieved.

During treatment adverse reactions were noted.

All the patients were advised to attend our OP department,2 weeks after treatment and the following parameters were assessed.

1. Symptomatic improvement
2. Hemoglobin
3. Haematocrit
4. MCV

- In our study, 18% (18/100) of the patients were < 20 years of age. 49% (49-100) of the patients 20% (20/100) of the patients were in the age group of 26-30 years and 13% (13/100) of the patients were >30 yrs. In our study, 56% of the patients were unbooked and 44% were booked. Booked and unbooked cases were equally distributed in 2 groups.

- In our study, 47% of women belonged to class V socio economic status and 46% belonged to Class IV socio economic status. Majority of the women with iron deficiency anaemia were in low socio economic group.

- In our study, 35% of patients were primipara and 52% were multipara.

- In our study, all patients (100%) experienced symptomatic improvement in both Iron sucrose group and blood transfusion group. There was no statistical difference between the two groups studied.

CHANGES IN HEMOGLOBIN.

In our study, hemoglobin level was measured before treatment and again after 2 weeks, post treatment assessment was done using sahli's hemoglobinometer at Kilpauk Medical College Hospital Laboratory.

Mean Hb in Group I and Group II was 7.49 gm/dl and 7.55 gm/dl respectively. Post treatment Hb after 2 weeks showed an mean Hb of 10.943 gm/dl and 11.096gm/dl respectively. An average rise in Hb was 3.44 gm/dl

and 3.51 gm/dl (P- 0.417) which was statistically not significant and the target Hb was achieved in 100% of women in both the groups studied.

Our study, similar to the study by Francoise bayoumeu et al (2005), Iron sucrose, apart from being more effective, Iron sucrose achieves the target levels in a short time. This paves the way for the other potential indications, such as anaemia discovered late in pregnancy or in patient who have low iron stores and present a risk of haemorrhage during postpartum, such as in multiple pregnancy or over distention of the uterus, in hope of avoiding a transfusion.

The average Hb rise in both the groups were same, hence iron sucrose is as effective as blood transfusion, in achieving the target hemoglobin in a shorter time.

The following studies in support of our study

S.No	**Name of the Study**	**Rise in Hb(gm/dl)**	**Our Study (Iron Sucrose)**
1	Wali et al 2002	3.8 gm/dl	3.4 gm/dl
2.	EJOG 1996[23]	3.2 gm/dl	3.4 gm/dl

CHANGE IN HAEMATOCRIT

In our study, the mean haematocrit in Group I and Group II was 28.4% and 30% respectively. Post treatment haematocrit assessment after 2 weeks showed an mean haematocrit value of 33.99% and 38.0% respectively. The P value is 0.1767 which was not statistically significant.

The average rise of haematocrit was 5.51% and 8.0% in Iron sucrose group and blood transfusion group, which was also not statistically significant.

The following studies in support of our study:

S.No	Name of the Study	Haematocrit	Our Study (Iron Sucrose)
1	Breymann et al 2005	↑	↑
2.	Dede et al (2005)[11]	↑	↑

CHANGE IN MCV

In our study, Mean MCV in Group I and Group II were 69.19 fl and 69.03 fl respectively. Post treatment MCV assessment, after 2 weeks showed mean MCV value of 86.69 fl and 86.01 fl respectively with P= .574,which was statistically not significant.

The average rise in MCV was 15.886 fl and 17.09 fl in Group I and Group II in the P value of 0.476 which was also not significant.

A study by Mrs. Khurshid Shabir Raja et al[30], journal of Pakistan Medical association, Vol. 28 showed mean MCV before treatment was 65 fl, mean MCV 3 weeks after treatment showed 75 fl and the mean rise in MCV was 10 fl with P value <0.5 which was statistically significant. This study was comparable with our study.

Adverse Reactions:

In our study, there was no adverse reactions in women treated with Iron sucrose for the treatment of Iron deficiency anaemia. On the otherhand, In Group II, patients treated with blood transfusion, there were more side effects, headache 2/50 (4%), chills and rigor 12/50 (24%), and Itching 8/50 (16%) of the patients.

Our study, similar to a observation, published in Journal of Transfusion Alternatives in transfusion medicine 9 (Supp 1.2) 13-18, which stated that blood transfusion for Iron deficiency anaemia is the most expensive and most hazardous form of therapy. Transfusion hazards are indeed numerous and well documented. The awareness of these risks of blood transfusion, together with the limited availability of blood due to

increasing shortages, should encourage physicians to seek alternative therapies to correct anaemia.[31]

The following studies in support of our study:

S.No	Name of the Study	Adverse Reactions	Our Study (Iron Sucrose)
1	Al Ra 2005	No	No
2.	Al Moment et al	No	No
3.	Hoigne et al	No	No

Gestational Age at delivery:

In our study, 10% of patients in Group I and 26% of patients in Group II delivered preterm. Though the incidence of preterm delivery is high in anaemia complicating pregnancy, the incidence of preterm delivery was high in the patients treated with blood transfusion, according to our study.

SUMMARY

In our study, 100 antenatal patients with iron deficiency anaemia attended to Kilpauk Medical College Hospital OP department between November 2009 to October 2010, selected according to the inclusion and exclusion criteria, already stated in methodology, were taken for this randomized controlled study. They were allocated into 2 groups of each with 50 antenatal patients.

GROUP I – Treated with Iron sucrose

GROUP II – Treated with Blood Transfusion

The results of the study are tabulated ,analysed and summarized as follows:-

1. Majority of the patients, around 49% belonged to the age group between 21-25 years in both Group I and Group II.
2. Booked and unbooked patients were equally distributed in both groups.
3. Majority (93%) of the women belonged to class IV and class V socio economic status in both Group I and Group II .
4. Both primi and multipara were equally distributed in both Group, 48% patients were primi and 52% were multipara.

5. All the patients (100%) in Group I and Group II had symptoms of easy fatiguability, breathlessness (Grade I), and pallor of skin and mucus membranes on examination.
6. Symptomatic improvement observed in all cases (100%) in both intravenous Iron sucrose group and blood transfusion group.
7. Mean rise in hemoglobin was 3.44 gm/dl in Intravenous iron sucrose group (Group I), 3.51 gm/dl in blood transfusion group (Group II). The gain in hemoglobin in both the groups were same.
8. Target Hb was achieved in 100% of patients in both group I and Group II.
9. Mean rise in haematocrit value was 5.5% in iron sucrose group (Group I) and 8.0% in blood transfusion group (Group II). The rise in haematocrit in both Group I, Group II were almost same, which was not statistically significant.
10. Mean rise in MCV was 17.49 fl and 17.09 fl in Group I and Group II respectively. The rise in MCV in both Group I and Group II were same.
11. The adverse effects were not at all observed in iron sucrose group (Group I) compared to 22% of the patients in blood transfusion group (Group II), P-0.000 value is which was statistically significant.
12. The incidence of preterm delivery was high in Blood transfusion Group II (26%) than in Group I (10%).

CONCLUSION

- Intravenous iron sucrose is as effective as blood transfusion, in improving hemoglobin, haematocrit values in the treatment of iron deficiency anemic during pregnancy.
- It is safe and well tolerated when compared to blood transfusion
- The adverse effects in intravenous iron sucrose treatment are not seen when compared to blood transfusion.
- The incidence of preterm delivery was high in patients treated with blood transfusion.
- Thus, it was concluded that, intra venous iron sucrose in the treatment of Iron deficiency anaemia in pregnancy is as effective as blood transfusion and it is safe, without adverse effects when compared to blood transfusion

PROFORMA

Name :

Age :

Obstetric Score :

Booking Status :

Socio Economic Status :

Chief Complaints :

H/o easy fatiguability

H/o breathlessness

H/o palpitation

H/o passing worms

H/o bleeding pr /hemetemesis/ hematuria

H/o bleeding diathesis

Past History

Any H/o Dm/HT/Bronchial Asthma/Cardia disease / thyroid disease /

General Examination:

Anaemia Dyspnoea jaundice

Pedal edema JVP

PR: BP: RR:

Systemic examination

Repiratory system

Cardio vascular system

Central nerovous System:

Obstetric Examination:

P/A: uterus- fundal height

FH-

INVESTIGATIONS:

1. Complete blood count

   Hb

   Haematocrit

   Total Count

   Differential count

   ESR

   Platelets

2. Peripheral smear
3. Urine- albumin

   Sugar

   Deposits

4. Blood Sugar
5. Blood Grouping & typing
6. VDRL
7. NVP
8. HBs Ag
9. BT
10. CT
11. Sr. Protein
12. MCV
13. Motion - Ova
    - Cyst

14. Urine – Culture – Sensitivity.
15. Obstetric Ultrasound

During Treatment

The following are monitored

1. PR
2. BP
3. Chills and rigor
4. Nausea and vomiting
5. Itching
6. Joint pain
7. Head ache,

8. Anaphylactic reaction

9. Urine output

Post treatment assessment after 2 weeks

1. Hb%
2. Haematocrit
3. MCV
4. Symptomatic Improvement.

Follow Up

GA at delivery : Term / pre term

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KEY TO MASTER CHART

S. No.	-	Serial Number
B	-	Booked
UB	-	Un Booked
GA	-	Gestational age.
SES	-	Socio Economic Status.
Hb	-	Hemoglobin in gm / dl
Pre	-	Prior to Iron Sucrose / Blood transfusion
Post	-	Post Treatment
MCV	-	Mean corpuscular Volume
OBST.Score	-	obstetric Score
Symp. Improvement	-	Symptomatic Improvement.
Easy fatig	-	Easy Fatiguability
G	-	Gravida
P	-	Para
L	-	Live Children
A	-	Abortion.
GA at delivery	-	Gestational age at delivery
T	-	Term delivery
PT	-	Preterm delivery
Gm/dl	-	gram per deciliter

LIST OF ABBREVIATIONS USED

Hb	-	Hemoglobin
gm/dl	-	gram / decilitre
mg	-	milligram
Fe^{++}	-	ferrous Ion
Fe^{+++}	-	Ferric Ion
ISC	-	Iron Sucrose complex
MCV	-	Mean corpuscular volume
RBC	-	red blood cell
I.V	-	intravenous
H/o	-	History of
Wks	-	weeks
FH	-	fetal heart
Bp	-	Blood pressure
PR	-	Pulse rate
GA	-	Gestational Age